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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/057,108

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Geert Plaetinck

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EXAMINER

SHIN, DANA H

ART UNIT

PAPER NUMBER

1635

MAIL DATE

DELIVERY MODE

10/27/2008

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/057,108	<b>Applicant(s)</b> PLAETINCK ET AL.	
	<b>Examiner</b> DANA SHIN	<b>Art Unit</b> 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 16 June 2008 and 29 August 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 13, 17-22, 25-27 and 54-56 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 13, 17-22, 25-27 and 54-56 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

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## **DETAILED ACTION**

### ***Status of Application/Amendment/Claims***

This Office action is in response to the communications filed on June 16, 2008 and August 29, 2008.

Currently, claims 13, 17-22, 25-27, and 54-56 are pending and under examination on the merits.

The following rejections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

### ***Response to Arguments and Amendments***

#### **Withdrawn Rejections**

Any rejections not repeated in this Office action are hereby withdrawn.

#### **Maintained Rejections**

#### ***Claim Rejections - 35 USC § 102***

Claim 20 remains rejected under 35 U.S.C. 102(a) as being anticipated by Fire et al. (WO 99/32619 A1) for the reasons of record as set forth in the Office action mailed on February 14, 2008 and for the reasons stated below.

Applicant's arguments filed on June 16, 2008 have been fully considered but they are not persuasive. Applicant argues that the Fire et al. provisional application does not disclose the instantly claimed expression vector and therefore applicant's invention precedes the priority date of Fire et al. based on the priority applications GB 9814536.0 and GB 9827152.1. However, the claimed T3 and SP6 promoters of claim 20 are first disclosed and described in the manner provided by the first paragraph of 35 U.S.C. in U.S. 09/347,311, which was filed on July 2, 1999. Hence, the priority date for claim 20 is granted only insofar as the filing date of 09/347,311, not the foreign priority documents. Since the WO patent of Fire et al. was published on July 1, 1999, which is prior to the filing date of 09/347,311, and therefore claim 20 remains rejected as being anticipated by Fire et al.

Claim 20 remains rejected under 35 U.S.C. 102(e) as being anticipated by Fire et al. (US 6,506,559 B1) for the reasons of record as set forth in the Office action mailed on February 14, 2008 and for the reasons stated below.

Applicant's arguments filed on June 16, 2008 have been fully considered but they are not persuasive. Applicant argues that the Fire et al. provisional application does not disclose the instantly claimed expression vector and therefore applicant's invention precedes the priority date of Fire et al. based on the priority applications GB 9814536.0 and GB 9827152.1. However, the claimed T3 and SP6 promoters of claim 20 are first disclosed and described in the manner provided by the first paragraph of 35 U.S.C. in U.S. 09/347,311, which was filed on July 2, 1999. Hence, the priority date for claim 20 is granted only insofar as the filing date of 09/347,311, not the foreign priority documents. Since the U.S. Application No. 09/215,257 for the US patent of

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Fire et al. was filed on December 18, 1998, which is prior to the filing date of 09/347,311, and therefore claim 20 remains rejected as being anticipated by the U.S. patent of Fire et al.

**New Rejections**

***Claim Rejections - 35 USC § 103***

Claims 13, 17-22, 25-27, and 54-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fire et al. (US 6,506,559 B1, citation of record) in view of Zdinak et al. (*Journal of Cellular Biochemistry*, 1997, 67:143-153), Talkad et al. (*Journal of Bacteriology*, 1978, 135:528-541, citation of record) and Noren et al. (US 5,691,140).

The claims are drawn to a method for down-regulating target gene expression in *C. elegans* comprising feeding *E. coli* that expresses dsRNA flanked by two promoters, wherein the promoters are selected from T7, T3, and SP6.

Fire et al. teach a method of down-regulating target gene expression in *C. elegans* by microinjecting an expression vector expressing a dsRNA driven by a promoter selected from T7, T3, and SP6 or a tissue-specific promoter such as the muscle-specific myo-3 promoter. Note that this teaching is disclosed and adequately supported in their priority document, US 60/068,562 filed on December 23, 1997. Fire et al. do not teach feeding *E. coli* expressing the dsRNA to *C. elegans*, nor do they teach that the dsRNA-containing expression vector comprises two promoters.

Zdinak et al. teach that one can express a transgene in *C. elegans* by feeding *E. coli* that expresses the transgene. In fact, they teach that *E. coli* has been the usual food source for experimental *C. elegans* in the art. See the entire reference.

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Talkad et al. teach *E. coli* strains that are deficient in RNase III. They teach that RNase III cleaves bacteriophage T7 RNAs as well as double-stranded RNAs.

Noren et al. teach bidirectional expression vectors comprising two opposing RNA polymerase promoters, wherein the promoters are of the same kind (e.g., T7 and T7) or of different kinds (e.g., SP6 and T7). They teach that such bidirectional expression vectors comprising two promoters in opposite direction allow efficient transcription of either strand of the inserted piece of RNA sequence. For example, they show that the sense strand (or top strand) of the inserted RNA sequence is transcribed by the promoter located at the 5' of the sense strand (that is, the promoter having a 'right' directionality), while the antisense strand (or bottom strand) is transcribed by the promoter located at the 3' of the sense strand (that is, the promoter having a 'left' directionality). Further, the bidirectional vectors are manufactured by a commercial vendor New England Biolabs, Inc. See columns 1-2; claims 1-2; Figures 1, 4B, 6-7.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to feed RNase III-deficient *E. coli* containing a bidirectional expression vector carrying a double-stranded RNA to *C. elegans*, in order to downregulate the expression of the RNA in *C. elegans*.

One of ordinary skill in the art would have been motivated to modify the RNAi-mediated downregulation of target gene expression in *C. elegans* of Fire et al. by incorporating the teachings of prior art, because the skilled artisan would have seen the advantage of doing so. For example, the skilled artisan would have seen the benefit in replacing the "microinjection" of *E. coli* containing an expression vector carrying a double-stranded RNA of Fire et al. with the "feeding" of *E. coli* of Zdinak et al., because one can express the double-stranded RNA in *C.*

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*elegans* without wasting the time and resources involved with microinjection, and because feeding *E. coli* to *C. elegans* was an art-recognized method for expressing transgenes in the *C. elegans*. Further, the skilled artisan would have seen the benefit in replacing the unidirectional expression vector of Fire et al. with the bidirectional expression vector of Noren et al., because bidirectional promoters were known to transcribe both sense and antisense strands, and because such bidirectional expression vector was commercially manufactured and available in the art. In addition, the skilled artisan would have seen the benefit in replacing the BL21/DE3 *E. coli* strain with the RNase III-negative *E. coli* strain of Talkad et al., because RNase III-negative *E. coli* strain, compared to RNase III-positive strain, would prevent the cleavage of the double-stranded RNA molecule, which must be expressed in the *C. elegans* that was fed the *E. coli*. Since the technology, materials, skills, and knowledge required to arrive at the claimed invention were all within the technical grasp of one of ordinary skill in the art, the skilled artisan would have had a reasonable expectation of success in modifying the invention of Fire et al. Accordingly, the claimed invention taken as a whole would have been *prima facie* obvious at the time of filing.

### ***Conclusion***

No claim is allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

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the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DANA SHIN whose telephone number is (571)272-8008. The examiner can normally be reached on Monday through Friday, from 7am-3:30pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Dana Shin  
Examiner  
Art Unit 1635

/J. E. Angell/  
Primary Examiner, Art Unit 1635